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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,719	09/20/2002	James Robl	103080-P08-058	2839
1473 7590 08/03/2007 FISH & NEAVE IP GROUP ROPES & GRAY LLP 1211 AVENUE OF THE AMERICAS NEW YORK, NY 10036-8704			EXAMINER TON, THAIAN N	
			ART UNIT 1632	PAPER NUMBER
			MAIL DATE 08/03/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

Application No.

10/070,719

Applicant(s)

ROBL ET AL.

Examiner

Thaian N. Ton

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 07 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 51-55 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 51-55 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

Applicants' Amendment and Response, filed 5/7/07, has been entered. Claim 51 is amended; claims 54-55 are newly added; claims 51-55 are pending and under current examination.

#### *Claim Objections*

The prior objection to claim 51 is withdrawn, in view of Applicants' amendment to the claim.

#### *Double Patenting*

The prior rejection of claims 1-17, 32-45 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4-11, 13-19, 24-30, 32-38, 40-52, 58-60 of copending Application No. 09/260,468 is rendered moot in view of the abandonment of this application.

The prior rejection of claims 1-17, 32-45 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-58 of copending Application No. 09/467,076 is rendered moot in view of the abandonment of this application.

The prior rejection of claims 1-17, 32-45 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 51, 52, 57, 62, 67, 69, 70 of copending Application No. 10/329,979 is withdrawn in view of Applicants' amendments.

Claims 51-53 and newly added claims 53-55 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/922,374. Applicants

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argue that they have now amended claim 51 to recite a method of producing a blastula or morula comprising the step of introducing mitochondria or mitochondrial DNA derived from cell(s) of the donor's cells' species. Applicants argue that the '374 application does not reflect the method of the instant claims. These arguments are not persuasive. The claims of the '374 case produce a blastula or morula by insertion of a desired human cell or cell nucleus. Thus, introduction of an entire human cell would encompass introducing mtDNA into the enucleated oocyte.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51-53 and newly added claims 54-55 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

*Applicants Arguments.* Applicants argue that the claims, as-amended, are not enabled because the specification teaches performing cross-species SCNT, and that although there are no working examples for the complete method of claim 51, there is an example of cross species SCNT, and a protocol for isolating mitochondria. Applicants argue that complete enablement of an invention does not require a working example, so long as the invention is disclosed such that one of skill in the

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art would be able to practice the claimed invention without undue experimentation. See page 6, 1<sup>st</sup> ¶ of the Response. Applicants argue that although there is a low efficiency in producing interspecies NT units, this does not evince unpredictability or undermine enablement, because the experimentation would not be undue. Applicants argue that the methods taught by the instant application are predictable and reproducible, as evidenced by Chang *et al.*, because Chang show cross-species NT by inserting human somatic nuclei into bovine oocytes, using the same methods as instantly-filed disclosure, therefore, Applicants argue, Chang supports Applicants' contention that the claimed invention is enabled. See pages 6-7 of the Response.

*Response To Arguments.* These arguments are considered, but are not persuasive. Applicants argue that the claimed invention is no longer drawn to the production of ES or stem-like cells, but are now directed to producing a morula or blastula. See page 8, 1<sup>st</sup> ¶. The Examiner responds that that the standard, under 112, 1<sup>st</sup> paragraph is to teach the skilled artisan how to make and use the claimed invention. Applicants elected method of producing embryonic or stem-like cells produced by their claimed methods. Although the claims have been amended to recite the production of a morula or blastula, there is no other enabled use that is contemplated by the specification within Applicants' election. That is, even if one of skill in the art were able to produce morula or blastula stage embryos utilizing Applicants' methods, one of skill in the art would have to practice undue experimentation to use the claimed invention for its contemplated purpose, within Applicants' elected invention, to produce embryonic or stem-like cells. There is no other use that is enabled for producing a morula or blastula embryo in the context of Applicants' invention; therefore, the rejection of record is maintained. See also, Roach & McNeish and Thomson with regard to the unpredictability in the art of producing embryonic stem cells.

Furthermore, with regard to the Chang reference, the Examiner responds that although Chang teach the production of blastocyst stage embryos, many of the blastocysts had abnormal number of chromosomes, and even in light of the production of normal embryos, it is clear that Chang *et al.* show that cross-species NT is an unpredictable process.

The Examiner maintains that the specification generally teaches the claimed method steps, but does not provide an enabling disclosure for the claimed invention. In particular, in light of the lack of an enabled use for the morula or blastula stage embryo produced by the claimed methods, as well as the unpredictability in the art with regard to the production of abnormal blastocysts in cross-species nuclear transfer, the lack of working examples provided, it would have required undue experimentation for one of ordinary skill in the art to practice the claimed invention.

*Applicants' Arguments.* With regard to the unpredictability in the art of donor-derived mitochondrial DNA in NT, Applicants argue that they do not need to identify the mechanism by which the claimed method works in order to satisfy the enablement requirement and the benefits of introducing donor-derived mitochondria or mitochondrial DNA do not necessarily require incorporation of the DNA into the oocyte. Applicants provide Mastromonaco *et al.* who suggest improved developmental competence of interspecific embryos may be achieved by introducing large numbers of donor mitochondria. See page 7 of the Response.

*Response To Arguments.* The Examiner agrees that Applicants need not identify the mechanism by which the claimed method works in order to satisfy the enablement requirement, however, the prior art of record clearly shows that cross-species nuclear transfer is unpredictable (see Wolfe, Gurdon, Meirelles, Dominko, Dominko (1999)), and further, that the introduction of mtDNA is unpredictable with regard to the further development of the NT unit (see Jiang and Chen). Thus, these unpredictabilities, coupled with the lack of an enabled use of the morula or blastula

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stage NT unit, fail to enable the claimed invention. The post-filing art of Mastromonaco *et al.* clearly show that cross species nuclear transfer remains unpredictable, state that, "A better understanding of the influence of the cytoplasmic environment on embryonic processes is necessary before somatic cell nuclear transfer can be considered a viable alternative for endangered species conservation." See last sentence of Abstract. Additionally, they show that even between close species, cross-species SCNT is highly unpredictable, see p. 4, 1<sup>st</sup> full ¶. Applicants' claims are directed to utilizing any differentiated human or mammalian donor cell into any enucleated animal oocyte of another species. This encompasses utilizing donor and recipient cells that are vastly different from each other. Mastromonaco do not teach that introduction of mitochondria improves embryonic processes, they speculate that, "Further studies are necessary to examine the specific mechanisms that are disrupted, such as mitochondrial differentiation and organization during embryo development and the subsequent changes in respiratory activity and ATP production, as well as the contribution of other cytoplasmic components to cell cycle regulation, including the centrosome and cytoskeletal network. Improved developmental competence of interspecific embryos may be achieved with the introduction of large numbers of donor mitochondria or other donor organelles of unknown significance at this time." See pages 22-23, bridging ¶. Thus, it is clear that they teach it would not be predictable nor known if the introduction of donor mitochondria, or other donor organelles, would achieve greater developmental competence. Mastromonaco provide evidence that even post-filing, cross-species SCNT remains unpredictable.

The specification is not enabling for the breadth of the claimed invention. The specification fails to overcome the above-recited unpredictabilities in cross-species nuclear transfer, the unpredictability in maintenance of the donor mtDNA, the importance of mtDNA in embryonic development, as well as in the production of embryonic or ES-like cells. One of skill in the art would not be able to practice the

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claimed invention, as broadly claimed, because the specification fails to provide guidance to practice the claimed invention, and the art provides significant teachings of the unpredictability found in the art, with regard to cross-species NT, and producing ES cells from the resultant NT unit. Because the intended use of the claimed method is to produce embryonic stem cells, one of skill in the art would recognize that the NT unit would need to be able to develop to blastocyst stage, with the expression of appropriate markers and karyotype, in order to produce ES cells. The specification provides no other enabled use for the morula or blastula, produced by the NT method, within the context of Applicants' claimed invention. Accordingly, it is maintained that it would have required undue experimentation for one of ordinary skill in the art to practice the claimed invention.

*Claim Rejections - 35 USC § 112*

The prior rejection of claim 51, under 35 U.S.C. 112, second paragraph, as being indefinite, is withdrawn in view of Applicants' amendment to the claim.



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*Conclusion*

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Thursday from 7:00 to 5:00 (Eastern Standard Time). Should the Examiner be unavailable, inquiries should be directed to Peter Paras, SPE of Art Unit 1632, at (571) 272-4517. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Thaian N. Ton/  
Primary Examiner  
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